

DOCKET NO.: BMS-2594

PATENT

Application No.: Not Yet Assigned

Preliminary Amendment - First Action Not Yet Received

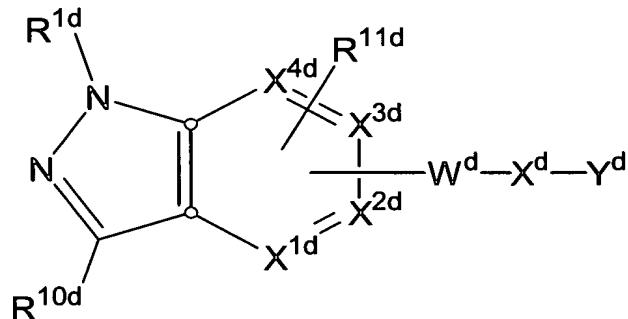
This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

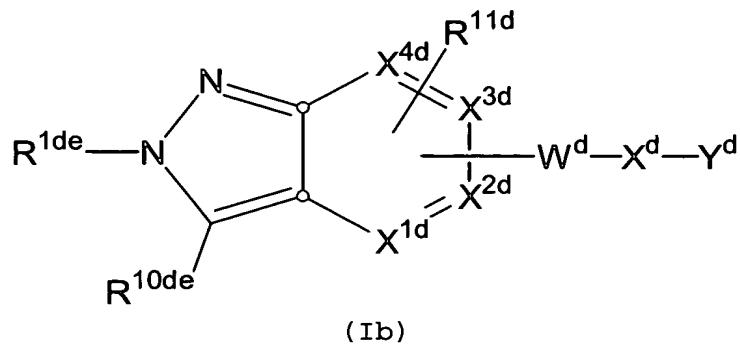
1. (Original) A compound, comprising: a targeting moiety and a chelator, wherein the targeting moiety is bound to the chelator, is a indazole nonpeptide, and binds to a receptor that is upregulated during angiogenesis and the compound has 0-1 linking groups between the targeting moiety and chelator.
2. (Original) A compound according to Claim 1, wherein the receptor is the integrin $\alpha_v\beta_3$ or $\alpha_v\beta_5$ and the compound is of the formula:

$(Q)_d-L_n-C_h$ or $(Q)_d-L_n-(C_h)_d$,

wherein, Q is independently a compound of Formula (Ia) or (Ib) :



(Ia)



including stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, or pharmaceutically acceptable salt or prodrug forms thereof wherein:

X^{1d} is N, CH, C- W^d - X^d - Y^d , or C- L_n ;

X^{2d} is N, CH, or C- W^d - X^d - Y^d ;

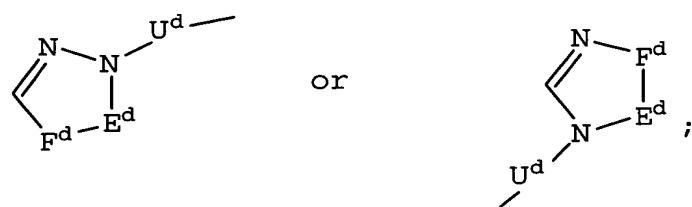
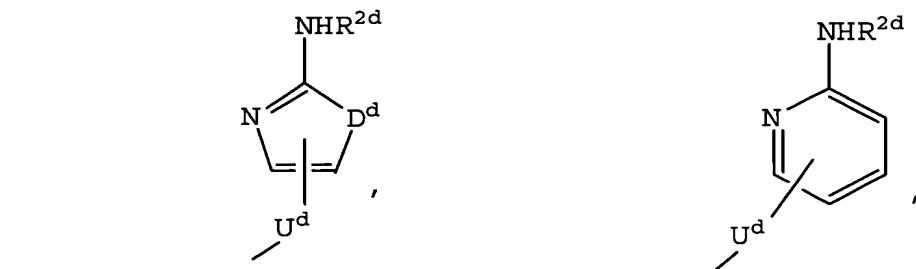
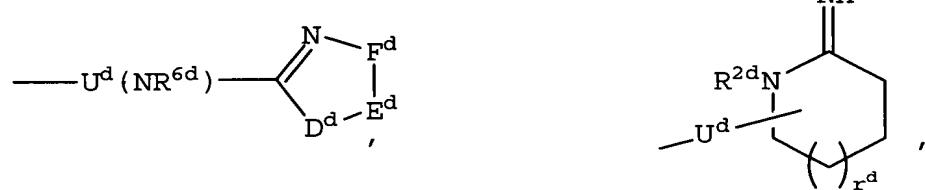
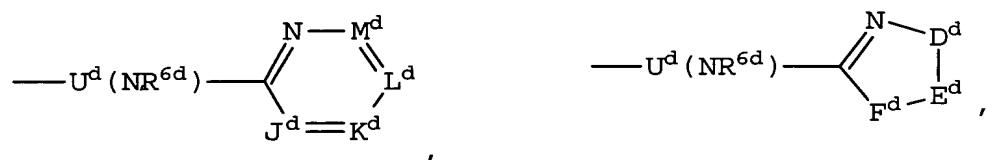
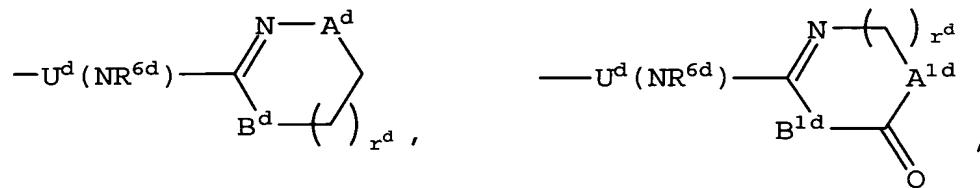
X^{3d} is N, CR^{11d}, or C- W^d - X^d - Y^d ;

X^{4d} is N or CR^{11d};

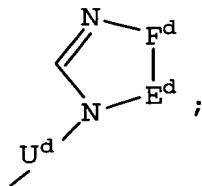
provided that when R^{1d} is R^{1de} then one of X^{1d} and X^{2d} is C- W^d - X^d - Y^d , and when R^{10d} is R^{1de} then X^{3d} is C- W^d - X^d - Y^d ;

R^{1d} is selected from: R^{1de} , C₁-C₆ alkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C₃-C₆ alkenyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C₃-C₇ cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C₄-C₁₁ cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , aryl substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d} , and aryl(C₁-C₆ alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d} ;

R^{1de} is selected from:



or



A^d and B^d are independently $-CH_2-$, $-O-$, $-N(R^{2d})-$, or $-C(=O)-$;

A^{1d} and B^{1d} are independently $-CH_2-$ or $-N(R^{3d})-$;

D^d is $-N(R^{2d})-$, $-O-$, $-S-$, $-C(=O)-$ or $-SO_2-$;

E^d-F^d is $-C(R^{4d})=C(R^{5d})-$, $-N=C(R^{4d})-$, $-C(R^{4d})=N-$, or
 $-C(R^{4d})_2C(R^{5d})_2-$;

J^d , K^d , L^d and M^d are independently selected from
 $-C(R^{4d})-$, $-C(R^{5d})-$ and $-N-$, provided that at least one of
 J^d , K^d , L^d and M^d is not $-N-$;

R^{2d} is selected from: H, C_1-C_6 alkyl, $(C_1-C_6$ alkyl)carbonyl,
 $(C_1-C_6$ alkoxy)carbonyl; $(C_1-C_6$ alkyl)aminocarbonyl, C_3-C_6
alkenyl, C_3-C_7 cycloalkyl, C_4-C_{11} cycloalkylalkyl, aryl,
heteroaryl(C_1-C_6 alkyl)carbonyl, heteroarylcarbonyl,
aryl(C_1-C_6 alkyl)-, $(C_1-C_6$ alkyl)carbonyl-, arylcarbonyl,
 C_1-C_6 alkylsulfonyl, arylsulfonyl, aryl(C_1-C_6
alkyl)sulfonyl, heteroarylsulfonyl, heteroaryl(C_1-C_6
alkyl)sulfonyl, aryloxycarbonyl, and aryl(C_1-C_6
alkoxy)carbonyl, wherein said aryl groups are substituted
with 0-2 substituents selected from the group: C_1-C_4
alkyl, C_1-C_4 alkoxy, halo, CF_3 , and nitro;

R^{3d} is selected from: H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_4-C_{11}
cycloalkylalkyl, aryl, aryl(C_1-C_6 alkyl)-, and
heteroaryl(C_1-C_6 alkyl)-;

R^{4d} and R^{5d} are independently selected from: H, C_1-C_4 alkoxy,
 $NR^{2d}R^{3d}$, halogen, NO_2 , CN , CF_3 , C_1-C_6 alkyl, C_3-C_6 alkenyl,

C_3 - C_7 cycloalkyl, C_4 - C_{11} cycloalkylalkyl, aryl, aryl(C_1 - C_6 alkyl)-, (C_1 - C_6 alkyl)carbonyl, (C_1 - C_6 alkoxy)carbonyl, and arylcarbonyl, or

alternatively, when substituents on adjacent atoms, R^{4d} and R^{5d} can be taken together with the carbon atoms to which they are attached to form a 5-7 membered carbocyclic or 5-7 membered heterocyclic aromatic or non-aromatic ring system, said carbocyclic or heterocyclic ring being optionally substituted with 0-2 groups selected from: C_1 - C_4 alkyl, C_1 - C_4 alkoxy, halo, cyano, amino, CF_3 , and NO_2 ;

U^d is selected from:

- $(CH_2)_n^{d-}$,
- $(CH_2)_n^d(CR^{7d}=CR^{8d})(CH_2)_m^{d-}$,
- $(CH_2)_n^d(C\equiv C)(CH_2)_m^{d-}$,
- $(CH_2)_t^dQ(CH_2)_m^{d-}$,
- $(CH_2)_n^dO(CH_2)_m^{d-}$,
- $(CH_2)_n^dN(R^{6d})(CH_2)_m^{d-}$,
- $(CH_2)_n^dC(=O)(CH_2)_m^{d-}$,
- $(CH_2)_n^d(C=O)N(R^{6d})(CH_2)_m^{d-}$
- $(CH_2)_n^dN(R^{6d})(C=O)(CH_2)_m^{d-}$, and
- $(CH_2)_n^dS(O)_p^d(CH_2)_m^{d-}$;

wherein one or more of the methylene groups in U^d is optionally substituted with R^{7d} ;

Q^d is selected from 1,2-cycloalkylene, 1,2-phenylene, 1,3-phenylene, 1,4-phenylene, 2,3-pyridinylene, 3,4-pyridinylene, 2,4-pyridinylene, and 3,4-pyridazinylene;

R^{6d} is selected from: H, C_1 - C_4 alkyl, and benzyl;

R^{7d} and R^{8d} are independently selected from: H, C_1 - C_6 alkyl, C_3 - C_7 cycloalkyl, C_4 - C_{11} cycloalkylalkyl, aryl, aryl(C_1 - C_6 alkyl)-, and heteroaryl(C_0 - C_6 alkyl)-;

R^{10d} is selected from: H, R^{1de} , C_1 - C_4 alkoxy substituted with 0-1 R^{21d} , $N(R^{6d})_2$, halogen, NO_2 , CN, CF_3 , CO_2R^{17d} , $C(=O)R^{17d}$, $CONR^{17d}R^{20d}$, $-SO_2R^{17d}$, C_1 - C_6 alkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_3 - C_6 alkenyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_3 - C_7 cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_4 - C_{11} cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , aryl substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d} , and aryl(C_1 - C_6 alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d} ;

R^{10de} is selected from: H, C_1 - C_4 alkoxy substituted with 0-1 R^{21d} , $N(R^{6d})_2$, halogen, NO_2 , CN, CF_3 , CO_2R^{17d} , $C(=O)R^{17d}$, $CONR^{17d}R^{20d}$, $-SO_2R^{17d}$, $-SO_2NR^{17d}R^{20d}$, C_1 - C_6 alkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_3 - C_6 alkenyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_3 - C_7 cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_4 - C_{11} cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , aryl substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d} , and aryl(C_1 - C_6 alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d} ;

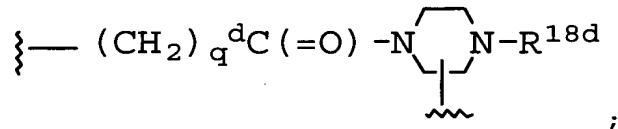
R^{11d} is selected from H, halogen, CF_3 , CN, NO_2 , hydroxy, $NR^{2d}R^{3d}$, C_1 - C_4 alkyl substituted with 0-1 R^{21d} , C_1 - C_4 alkoxy substituted with 0-1 R^{21d} , aryl substituted with 0-

1 R^{21d} , aryl (C_1-C_6 alkyl) - substituted with 0-1 R^{21d} , (C_1-C_4 alkoxy) carbonyl substituted with 0-1 R^{21d} , (C_1-C_4 alkyl) carbonyl substituted with 0-1 R^{21d} , C_1-C_4 alkylsulfonyl substituted with 0-1 R^{21d} , and C_1-C_4 alkylaminosulfonyl substituted with 0-1 R^{21d} ;

W^d is selected from:

- $(C(R^{12d})_2)_q^{d}C(=O)N(R^{13d})-$, and
- $C(=O)-N(R^{13d})-(C(R^{12d})_2)_q^{d}-$;

X^d is $-C(R^{12d})(R^{14d})-C(R^{12d})(R^{15d})-$; or
alternatively, W^d and X^d can be taken together to be



R^{12d} is selected from H, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, C_4-C_{10} cycloalkylalkyl, (C_1-C_4 alkyl) carbonyl, aryl, and aryl (C_1-C_6 alkyl) -;

R^{13d} is selected from H, C_1-C_6 alkyl, C_3-C_7 cycloalkylmethyl, and aryl (C_1-C_6 alkyl) -;

R^{14d} is selected from:

H, C_1-C_6 alkylthio (C_1-C_6 alkyl) -, aryl (C_1-C_{10} alkylthioalkyl) -, aryl (C_1-C_{10} alkoxyalkyl) -, C_1-C_{10} alkyl, C_1-C_{10} alkoxyalkyl, C_1-C_6 hydroxyalkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, C_3-C_{10} cycloalkyl, C_3-C_{10} cycloalkylalkyl, aryl (C_1-C_6 alkyl) -, heteroaryl (C_1-C_6 alkyl) -, aryl, heteroaryl, CO_2R^{17d} , $C(=O)R^{17d}$, and $CONR^{17d}R^{20d}$, provided

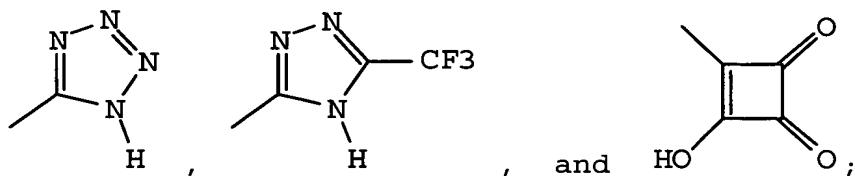
that any of the above alkyl, cycloalkyl, aryl or heteroaryl groups may be unsubstituted or substituted independently with 0-1 R^{16d} or 0-2 R^{11d} ;

R^{15d} is selected from:

H, R^{16d} , C_1-C_{10} alkyl, C_1-C_{10} alkoxyalkyl, C_1-C_{10} alkylaminoalkyl, C_1-C_{10} dialkylaminoalkyl, (C_1-C_{10} alkyl)carbonyl, aryl(C_1-C_6 alkyl)carbonyl, C_1-C_{10} alkenyl, C_1-C_{10} alkynyl, C_3-C_{10} cycloalkyl, C_3-C_{10} cycloalkylalkyl, aryl(C_1-C_6 alkyl)-, heteroaryl(C_1-C_6 alkyl)-, aryl, heteroaryl, CO_2R^{17d} , $C(=O)R^{17d}$, $CONR^{17d}R^{20d}$, SO_2R^{17d} , and $SO_2NR^{17d}R^{20d}$, provided that any of the above alkyl, cycloalkyl, aryl or heteroaryl groups may be unsubstituted or substituted independently with 0-2 R^{11d} ;

Y^d is selected from:

- COR^{19d} , - SO_3H , - PO_3H , tetrazolyl, - $CONHNHSO_2CF_3$, - $CONHSO_2R^{17d}$, - $CONHSO_2NHR^{17d}$, - $NHCOCF_3$, - $NHCONHSO_2R^{17d}$, - $NHSO_2R^{17d}$, - OPO_3H_2 , - OSO_3H , - PO_3H_2 , - SO_3H , - SO_2NHCOR^{17d} , - $SO_2NHCO_2R^{17d}$,



R^{16d} is selected from:

- $N(R^{20d})-C(=O)-O-R^{17d}$,
- $N(R^{20d})-C(=O)-R^{17d}$,
- $N(R^{20d})-C(=O)-NH-R^{17d}$,
- $N(R^{20d})SO_2-R^{17d}$, and
- $N(R^{20d})SO_2-NR^{20d}R^{17d}$;

R^{17d} is selected from:

C₁-C₁₀ alkyl optionally substituted with a bond to L_n, C₃-C₁₁ cycloalkyl optionally substituted with a bond to L_n, aryl(C₁-C₆ alkyl)- optionally substituted with a bond to L_n, (C₁-C₆ alkyl)aryl optionally substituted with a bond to L_n, heteroaryl(C₁-C₆ alkyl)- optionally substituted with a bond to L_n, (C₁-C₆ alkyl)heteroaryl optionally substituted with a bond to L_n, biaryl(C₁-C₆ alkyl)- optionally substituted with a bond to L_n, heteroaryl optionally substituted with a bond to L_n, aryl optionally substituted with a bond to L_n, biaryl optionally substituted with a bond to L_n, and a bond to L_n, wherein said aryl, biaryl or heteroaryl groups are also optionally substituted with 0-3 substituents selected from the group consisting of: C₁-C₄ alkyl, C₁-C₄ alkoxy, aryl, heteroaryl, halo, cyano, amino, CF₃, and NO₂;

R^{18d} is selected from:

-H,
-C(=O)-O-R^{17d},
-C(=O)-R^{17d},
-C(=O)-NH-R^{17d},
-SO₂-R^{17d}, and
-SO₂-NR^{20d}R^{17d};

R^{19d} is selected from: hydroxy, C₁-C₁₀ alkyloxy, C₃-C₁₁ cycloalkyloxy, aryloxy, aryl(C₁-C₆ alkoxy)-, C₃-C₁₀ alkylcarbonyloxyalkyloxy, C₃-C₁₀ alkoxy carbonyloxyalkyloxy, C₂-C₁₀ alkoxy carbonylalkyloxy, C₅-C₁₀ cycloalkylcarbonyloxyalkyloxy,

C_5-C_{10} cycloalkoxycarbonyloxyalkyloxy,
 C_5-C_{10} cycloalkoxycarbonylalkyloxy,
 C_7-C_{11} aryloxycarbonylalkyloxy,
 C_8-C_{12} aryloxycarbonyloxyalkyloxy,
 C_8-C_{12} arylcarbonyloxyalkyloxy,
 C_5-C_{10} alkoxyalkylcarbonyloxyalkyloxy, C_5-C_{10} (5-alkyl-
1,3-dioxa-cyclopenten-2-one-yl)methyloxy, $C_{10}-C_{14}$ (5-aryl-
1,3-dioxa-cyclopenten-2-one-yl)methyloxy, and
 $(R^{11d})(R^{12d})N-(C_1-C_{10} \text{ alkoxy})-$;

R^{20d} is selected from: H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_4-C_{11}
cycloalkylalkyl, aryl, aryl(C_1-C_6 alkyl)-, and
heteroaryl(C_1-C_6 alkyl)-;

R^{21d} is selected from: COOH and $NR^{6d}{}_2$;

m^d is 0-4 ;

n^d is 0-4 ;

t^d is 0-4 ;

p^d is 0-2 ;

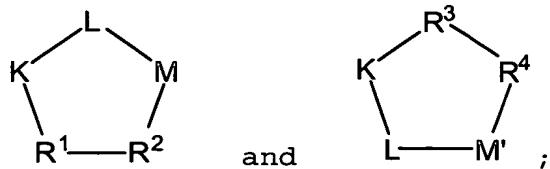
q^d is 0-2 ; and

r^d is 0-2 ;

with the following provisos:

- (1) t^d , n^d , m^d and q^d are chosen such that the number of atoms connecting R^{1d} and Y^d is in the range of 10-14; and
- (2) n^d and m^d are chosen such that the value of n^d plus m^d is greater than one unless U^d is
 $-(CH_2)_t^d Q^d (CH_2)_m^d-$;

or Q is a peptide selected from the group:



R¹ is L-valine, D-valine or L-lysine optionally substituted on the ε amino group with a bond to L_n;

R² is L-phenylalanine, D-phenylalanine, D-1-naphthylalanine, 2-aminothiazole-4-acetic acid or tyrosine, the tyrosine optionally substituted on the hydroxy group with a bond to L_n;

R³ is D-valine;

R⁴ is D-tyrosine substituted on the hydroxy group with a bond to L_n;

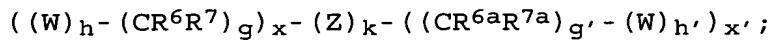
provided that one of R¹ and R² in each Q is substituted with a bond to L_n, and further provided that when R² is 2-aminothiazole-4-acetic acid, K is N-methylarginine;

provided that at least one Q is a compound of Formula (Ia) or (Ib);

d is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

d' is 1-100;

L_n is a linking group having the formula:



W is independently selected at each occurrence from the group:

O, S, NH, NHC(=O), C(=O)NH, NR⁸C(=O), C(=O)N R⁸, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO₂, SO₂NH, (OCH₂CH₂)_s, (CH₂CH₂O)_{s'}, (OCH₂CH₂CH₂)_{s''}, (CH₂CH₂CH₂O)_t, and (aa)_{t'};

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R¹⁰, C₃₋₁₀ cycloalkyl substituted with 0-3 R¹⁰, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁰;

R⁶, R^{6a}, R⁷, R^{7a}, and R⁸ are independently selected at each occurrence from the group: H, =O, COOH, SO₃H, PO₃H, C_{1-C5} alkyl substituted with 0-3 R¹⁰, aryl substituted with 0-3 R¹⁰, benzyl substituted with 0-3 R¹⁰, and C_{1-C5} alkoxy substituted with 0-3 R¹⁰, NHC(=O)R¹¹, C(=O)NHR¹¹, NHC(=O)NHR¹¹, NHR¹¹, R¹¹, and a bond to Ch;

R¹⁰ is independently selected at each occurrence from the group: a bond to Ch, COOR¹¹, C(=O)NHR¹¹, NHC(=O)R¹¹, OH, NHR¹¹, SO₃H, PO₃H, -OPO₃H₂, -OSO₃H, aryl substituted with 0-3 R¹¹, C₁₋₅ alkyl substituted with 0-1 R¹², C₁₋₅ alkoxy substituted with 0-1 R¹², and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹¹;

R¹¹ is independently selected at each occurrence from the group: H, alkyl substituted with 0-1 R¹², aryl substituted with 0-1 R¹², a 5-10 membered heterocyclic

ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R¹², C₃₋₁₀ cycloalkyl substituted with 0-1 R¹², polyalkylene glycol substituted with 0-1 R¹², carbohydrate substituted with 0-1 R¹², cyclodextrin substituted with 0-1 R¹², amino acid substituted with 0-1 R¹², polycarboxyalkyl substituted with 0-1 R¹², polyazaalkyl substituted with 0-1 R¹², and peptide substituted with 0-1 R¹², wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to C_h;

R¹² is a bond to C_h;

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;

h' is selected from 0, 1, and 2;

g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s'' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

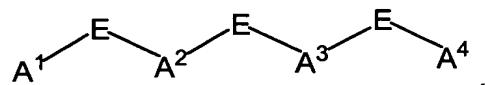
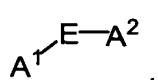
t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

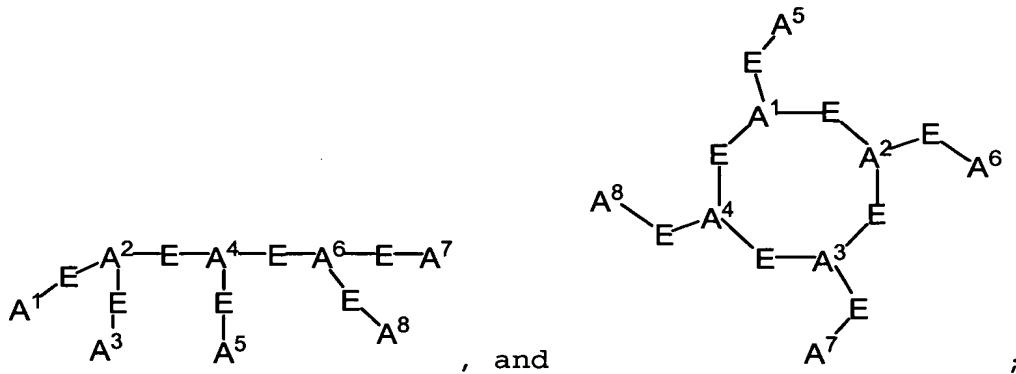
t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

x is selected from 0, 1, 2, 3, 4, and 5;

x' is selected from 0, 1, 2, 3, 4, and 5;

C_h is a metal bonding unit having a formula selected from the group:





A^1 , A^2 , A^3 , A^4 , A^5 , A^6 , A^7 , and A^8 are independently selected at each occurrence from the group: NR^{13} , $NR^{13}R^{14}$, S , SH , $S(Pg)$, O , OH , PR^{13} , $PR^{13}R^{14}$, $P(O)R^{15}R^{16}$, and a bond to L_n ;

E is a bond, CH , or a spacer group independently selected at each occurrence from the group: C_1-C_{10} alkyl substituted with 0-3 R^{17} , aryl substituted with 0-3 R^{17} , C_{3-10} cycloalkyl substituted with 0-3 R^{17} , heterocyclo- C_{1-10} alkyl substituted with 0-3 R^{17} , wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N , S , and O , C_{6-10} aryl- C_{1-10} alkyl substituted with 0-3 R^{17} , C_{1-10} alkyl- C_{6-10} aryl- substituted with 0-3 R^{17} , and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N , S , and O and substituted with 0-3 R^{17} ;

R^{13} and R^{14} are each independently selected from the group: a bond to L_n , hydrogen, C_1-C_{10} alkyl substituted with 0-3 R^{17} , aryl substituted with 0-3 R^{17} , C_{1-10} cycloalkyl substituted with 0-3 R^{17} , heterocyclo- C_{1-10} alkyl substituted with 0-3 R^{17} , wherein the heterocyclo group

is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C₆-₁₀ aryl-C₁-₁₀ alkyl substituted with 0-3 R¹⁷, C₁-₁₀ alkyl-C₆-₁₀ aryl- substituted with 0-3 R¹⁷, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁷, and an electron, provided that when one of R¹³ or R¹⁴ is an electron, then the other is also an electron;

alternatively, R¹³ and R¹⁴ combine to form =C(R²⁰)(R²¹);

R¹⁵ and R¹⁶ are each independently selected from the group: a bond to L_n, -OH, C₁-C₁₀ alkyl substituted with 0-3 R¹⁷, C₁-C₁₀ alkyl substituted with 0-3 R¹⁷, aryl substituted with 0-3 R¹⁷, C₃-₁₀ cycloalkyl substituted with 0-3 R¹⁷, heterocyclo-C₁-₁₀ alkyl substituted with 0-3 R¹⁷, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C₆-₁₀ aryl-C₁-₁₀ alkyl substituted with 0-3 R¹⁷, C₁-₁₀ alkyl-C₆-₁₀ aryl- substituted with 0-3 R¹⁷, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁷;

R¹⁷ is independently selected at each occurrence from the group: a bond to L_n, =O, F, Cl, Br, I, -CF₃, -CN, -CO₂R¹⁸, -C(=O)R¹⁸, -C(=O)N(R¹⁸)₂, -CHO, -CH₂OR¹⁸, -OC(=O)R¹⁸, -OC(=O)OR^{18a}, -OR¹⁸, -OC(=O)N(R¹⁸)₂, -NR¹⁹C(=O)R¹⁸, -NR¹⁹C(=O)OR^{18a}, -NR¹⁹C(=O)N(R¹⁸)₂,

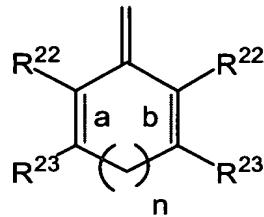
-NR¹⁹SO₂N(R¹⁸)₂, -NR¹⁹SO₂R^{18a}, -SO₃H, -SO₂R^{18a}, -SR¹⁸,
-S(=O)R^{18a}, -SO₂N(R¹⁸)₂, -N(R¹⁸)₂, -NHC(=S)NHR¹⁸, =NOR¹⁸,
NO₂, -C(=O)NHOR¹⁸, -C(=O)NHNR¹⁸R^{18a}, -OCH₂CO₂H,
2-(1-morpholino)ethoxy, C₁-C₅ alkyl, C₂-C₄ alkenyl, C₃-C₆
cycloalkyl, C₃-C₆ cycloalkylmethyl, C₂-C₆ alkoxyalkyl,
aryl substituted with 0-2 R¹⁸, and a 5-10 membered
heterocyclic ring system containing 1-4 heteroatoms
independently selected from N, S, and O;

R¹⁸, R^{18a}, and R¹⁹ are independently selected at each
occurrence from the group: a bond to L_n, H, C₁-C₆ alkyl,
phenyl, benzyl, C₁-C₆ alkoxy, halide, nitro, cyano, and
trifluoromethyl;

Pg is a thiol protecting group;

R²⁰ and R²¹ are independently selected from the group: H,
C₁-C₁₀ alkyl, -CN, -CO₂R²⁵, -C(=O)R²⁵, -C(=O)N(R²⁵)₂,
C₂-C₁₀ 1-alkene substituted with 0-3 R²³, C₂-C₁₀ 1-alkyne
substituted with 0-3 R²³, aryl substituted with 0-3 R²³,
unsaturated 5-10 membered heterocyclic ring system
containing 1-4 heteroatoms independently selected from N,
S, and O and substituted with 0-3 R²³, and unsaturated
C₃-C₁₀ carbocycle substituted with 0-3 R²³;

alternatively, R²⁰ and R²¹, taken together with the divalent
carbon radical to which they are attached form:



R^{22} and R^{23} are independently selected from the group: H, R^{24} , C_1-C_{10} alkyl substituted with 0-3 R^{24} , C_2-C_{10} alkenyl substituted with 0-3 R^{24} , C_2-C_{10} alkynyl substituted with 0-3 R^{24} , aryl substituted with 0-3 R^{24} , a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{24} , and C_{3-10} carbocycle substituted with 0-3 R^{24} ;

alternatively, R^{22} , R^{23} taken together form a fused aromatic or a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O;

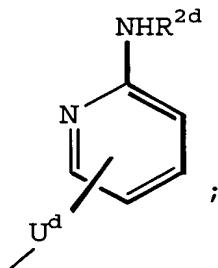
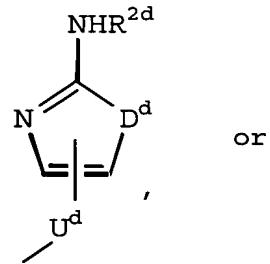
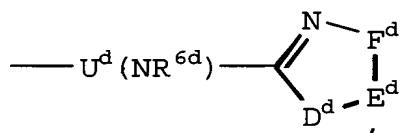
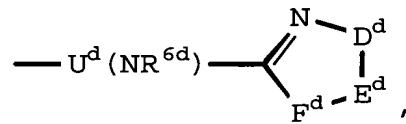
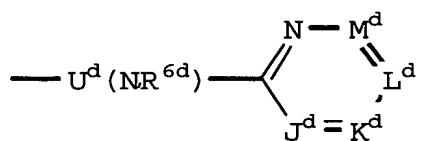
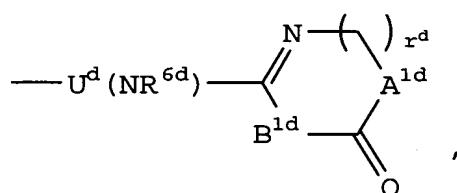
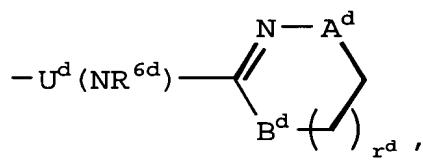
a and **b** indicate the positions of optional double bonds and **n** is 0 or 1;

R^{24} is independently selected at each occurrence from the group: =O, F, Cl, Br, I, $-CF_3$, $-CN$, $-CO_2R^{25}$, $-C(=O)R^{25}$, $-C(=O)N(R^{25})_2$, $-N(R^{25})_3^+$, $-CH_2OR^{25}$, $-OC(=O)R^{25}$, $-OC(=O)OR^{25a}$, $-OR^{25}$, $-OC(=O)N(R^{25})_2$, $-NR^{26}C(=O)R^{25}$, $-NR^{26}C(=O)OR^{25a}$, $-NR^{26}C(=O)N(R^{25})_2$, $-NR^{26}SO_2N(R^{25})_2$, $-NR^{26}SO_2R^{25a}$, $-SO_3H$, $-SO_2R^{25a}$, $-SR^{25}$, $-S(=O)R^{25a}$, $-SO_2N(R^{25})_2$, $-N(R^{25})_2$, $=NOR^{25}$, $-C(=O)NHOR^{25}$, $-OCH_2CO_2H$, and 2-(1-morpholino)ethoxy; and,

R^{25} , R^{25a} , and R^{26} are each independently selected at each occurrence from the group: hydrogen and C₁-C₆ alkyl.

3. (Original) A compound according to Claim 2, wherein:

R^{1de} is selected from:



A^d and B^d are independently -CH₂-, -O-, -N(R^{2d})-, or -C(=O)-;

A^{1d} and B^{1d} are independently $-CH_2-$ or $-N(R^{3d})-$;

D^d is $-N(R^{2d})-$, $-O-$, $-S-$, $-C(=O)-$ or $-SO_2-$;

E^{d-F^d} is $-C(R^{4d})=C(R^{5d})-$, $-N=C(R^{4d})-$, $-C(R^{4d})=N-$, or $-C(R^{4d})_2C(R^{5d})_2-$;

J^d , K^d , L^d and M^d are independently selected from: $C(R^{4d})-$, $-C(R^{5d})-$ and $-N-$, provided that at least one of J^d , K^d , L^d and M^d is not $-N-$;

R^{2d} is selected from: H, C_1-C_6 alkyl, $(C_1-C_6$ alkyl) carbonyl, $(C_1-C_6$ alkoxy) carbonyl, C_1-C_6 alkylaminocarbonyl, C_3-C_6 alkenyl, C_3-C_7 cycloalkyl, C_4-C_{11} cycloalkylalkyl, aryl, heteroaryl(C_1-C_6 alkyl) carbonyl, heteroarylcarbonyl, aryl(C_1-C_6 alkyl)-, $(C_1-C_6$ alkyl) carbonyl, arylcarbonyl, alkylsulfonyl, arylsulfonyl, aryl(C_1-C_6 alkyl) sulfonyl, heteroarylsulfonyl, heteroaryl(C_1-C_6 alkyl) sulfonyl, aryloxycarbonyl, and aryl(C_1-C_6 alkoxy) carbonyl, wherein said aryl groups are substituted with 0-2 substituents selected from the group consisting of C_1-C_4 alkyl, C_1-C_4 alkoxy, halo, CF_3 , and nitro;

R^{3d} is selected from: H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_4-C_{11} cycloalkylalkyl, aryl, aryl(C_1-C_6 alkyl)-, and heteroaryl(C_1-C_6 alkyl)-;

R^{4d} and R^{5d} are independently selected from: H, C_1-C_4 alkoxy, $NR^{2d}R^{3d}$, halogen, NO_2 , CN , CF_3 , C_1-C_6 alkyl, C_3-C_6 alkenyl,

C_3-C_7 cycloalkyl, C_4-C_{11} cycloalkylalkyl, aryl, aryl(C_1-C_6 alkyl)-, C_2-C_7 alkylcarbonyl, and arylcarbonyl;

alternatively, when substituents on adjacent atoms, R^{4d} and R^{5d} can be taken together with the carbon atoms to which they are attached to form a 5-7 membered carbocyclic or 5-7 membered heterocyclic aromatic or non-aromatic ring system, said carbocyclic or heterocyclic ring being optionally substituted with 0-2 groups selected from: C_1-C_4 alkyl, C_1-C_4 alkoxy, halo, cyano, amino, CF_3 , or NO_2 ;

U^d is selected from:

- $(CH_2)_n^d$ -,
- $(CH_2)_n^d (CR^{7d}=CR^{8d}) (CH_2)_m^d$ -,
- $(CH_2)_t^d Q^d (CH_2)_m^d$ -,
- $(CH_2)_n^d O (CH_2)_m^d$ -,
- $(CH_2)_n^d N(R^{6d}) (CH_2)_m^d$ -,
- $(CH_2)_n^d C(=O) (CH_2)_m^d$ -, and
- $(CH_2)_n^d S(O)_p^d (CH_2)_m^d$ -;

wherein one or more of the methylene groups in U^d is optionally substituted with R^{7d} ;

Q^d is selected from 1,2-phenylene, 1,3-phenylene, 2,3-pyridinylene, 3,4-pyridinylene, and 2,4-pyridinylene;

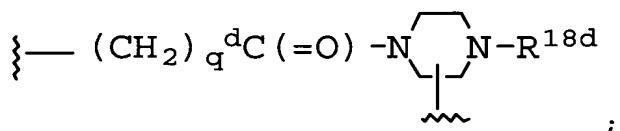
R^{6d} is selected from: H, C_1-C_4 alkyl, and benzyl;

R^{7d} and R^{8d} are independently selected from: H, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₄-C₁₁ cycloalkylalkyl, aryl, aryl(C₁-C₆ alkyl)-, and heteroaryl(C₀-C₆ alkyl)-;

w^d is $-C(=O)-N(R^{13d})-(C(R^{12d})_2)_q^d$;

x^d is $-C(R^{12d}) (R^{14d}) - C(R^{12d}) (R^{15d}) -$;

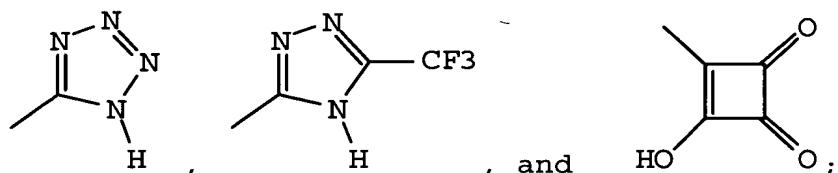
alternatively, w^d and x^d can be taken together to be



R^{12d} is H or C₁-C₆ alkyl;

y^d is selected from:

-COR^{19d}, -SO₃H,



d is selected from 1, 2, 3, 4, and 5;

d' is 1-50;

W is independently selected at each occurrence from the group:
 O , NH , $NHC(=O)$, $C(=O)NH$, $NR^8C(=O)$, $C(=O)N R^8$, $C(=O)$,

$\text{C}(=\text{O})\text{O}$, $\text{OC}(=\text{O})$, $\text{NHC}(=\text{S})\text{NH}$, $\text{NHC}(=\text{O})\text{NH}$, SO_2 , $(\text{OCH}_2\text{CH}_2)_s$,
 $(\text{CH}_2\text{CH}_2\text{O})_{s'}$, $(\text{OCH}_2\text{CH}_2\text{CH}_2)_{s''}$, $(\text{CH}_2\text{CH}_2\text{CH}_2\text{O})_t$, and $(\text{aa})_{t'}$;

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-1 R^{10} ,
 C_{3-10} cycloalkyl substituted with 0-1 R^{10} , and a 5-10
membered heterocyclic ring system containing 1-4
heteroatoms independently selected from N, S, and O and
substituted with 0-1 R^{10} ;

R^6 , R^{6a} , R^7 , R^{7a} , and R^8 are independently selected at each
occurrence from the group: H, $=\text{O}$, COOH , SO_3H , $\text{C}_1\text{-C}_5$ alkyl
substituted with 0-1 R^{10} , aryl substituted with 0-1 R^{10} ,
benzyl substituted with 0-1 R^{10} , and $\text{C}_1\text{-C}_5$ alkoxy
substituted with 0-1 R^{10} , $\text{NHC}(=\text{O})\text{R}^{11}$, $\text{C}(=\text{O})\text{NHR}^{11}$,
 $\text{NHC}(=\text{O})\text{NHR}^{11}$, NHR^{11} , R^{11} , and a bond to C_h ;

k is 0 or 1;

s is selected from 0, 1, 2, 3, 4, and 5;

s' is selected from 0, 1, 2, 3, 4, and 5;

s'' is selected from 0, 1, 2, 3, 4, and 5;

t is selected from 0, 1, 2, 3, 4, and 5;

A^1 , A^2 , A^3 , A^4 , A^5 , A^6 , A^7 , and A^8 are independently selected at
each occurrence from the group: NR^{13} , $\text{NR}^{13}\text{R}^{14}$, S, SH,
 $\text{S}(\text{Pg})$, OH, and a bond to L_n ;

E is a bond, CH, or a spacer group independently selected at
each occurrence from the group: $\text{C}_1\text{-C}_{10}$ alkyl substituted
with 0-3 R^{17} , aryl substituted with 0-3 R^{17} , C_{3-10}
cycloalkyl substituted with 0-3 R^{17} , and a 5-10 membered
heterocyclic ring system containing 1-4 heteroatoms

independently selected from N, S, and O and substituted with 0-3 R¹⁷;

R¹³ and R¹⁴ are each independently selected from the group: a bond to L_n, hydrogen, C₁-C₁₀ alkyl substituted with 0-3 R¹⁷, aryl substituted with 0-3 R¹⁷, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁷, and an electron, provided that when one of R¹³ or R¹⁴ is an electron, then the other is also an electron;

alternatively, R¹³ and R¹⁴ combine to form =C(R²⁰)(R²¹);

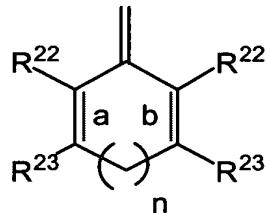
R¹⁷ is independently selected at each occurrence from the group: a bond to L_n, =O, F, Cl, Br, I, -CF₃, -CN, -CO₂R¹⁸, -C(=O)R¹⁸, -C(=O)N(R¹⁸)₂, -CH₂OR¹⁸, -OC(=O)R¹⁸, -OC(=O)OR^{18a}, -OR¹⁸, -OC(=O)N(R¹⁸)₂, -NR¹⁹C(=O)R¹⁸, -NR¹⁹C(=O)OR^{18a}, -NR¹⁹C(=O)N(R¹⁸)₂, -NR¹⁹SO₂N(R¹⁸)₂, -NR¹⁹SO₂R^{18a}, -SO₃H, -SO₂R^{18a}, -S(=O)R^{18a}, -SO₂N(R¹⁸)₂, -N(R¹⁸)₂, -NHC(=S)NHR¹⁸, =NOR¹⁸, -C(=O)NHNR¹⁸R^{18a}, -OCH₂CO₂H, and 2-(1-morpholino)ethoxy;

R¹⁸, R^{18a}, and R¹⁹ are independently selected at each occurrence from the group: a bond to L_n, H, and C₁-C₆ alkyl;

R²⁰ and R²¹ are independently selected from the group: H, C₁-C₅ alkyl, -CO₂R²⁵, C₂-C₅ 1-alkene substituted with 0-3 R²³, C₂-C₅ 1-alkyne substituted with 0-3 R²³, aryl substituted with 0-3 R²³, and unsaturated 5-10 membered heterocyclic ring system containing 1-4 heteroatoms

independently selected from N, S, and O and substituted with 0-3 R²³;

alternatively, R²⁰ and R²¹, taken together with the divalent carbon radical to which they are attached form:



R²² and R²³ are independently selected from the group: H, and R²⁴;

alternatively, R²², R²³ taken together form a fused aromatic or a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O;

R²⁴ is independently selected at each occurrence from the group: -CO₂R²⁵, -C(=O)N(R²⁵)₂, -CH₂OR²⁵, -OC(=O)R²⁵, -OR²⁵, -SO₃H, -N(R²⁵)₂, and -OCH₂CO₂H; and,

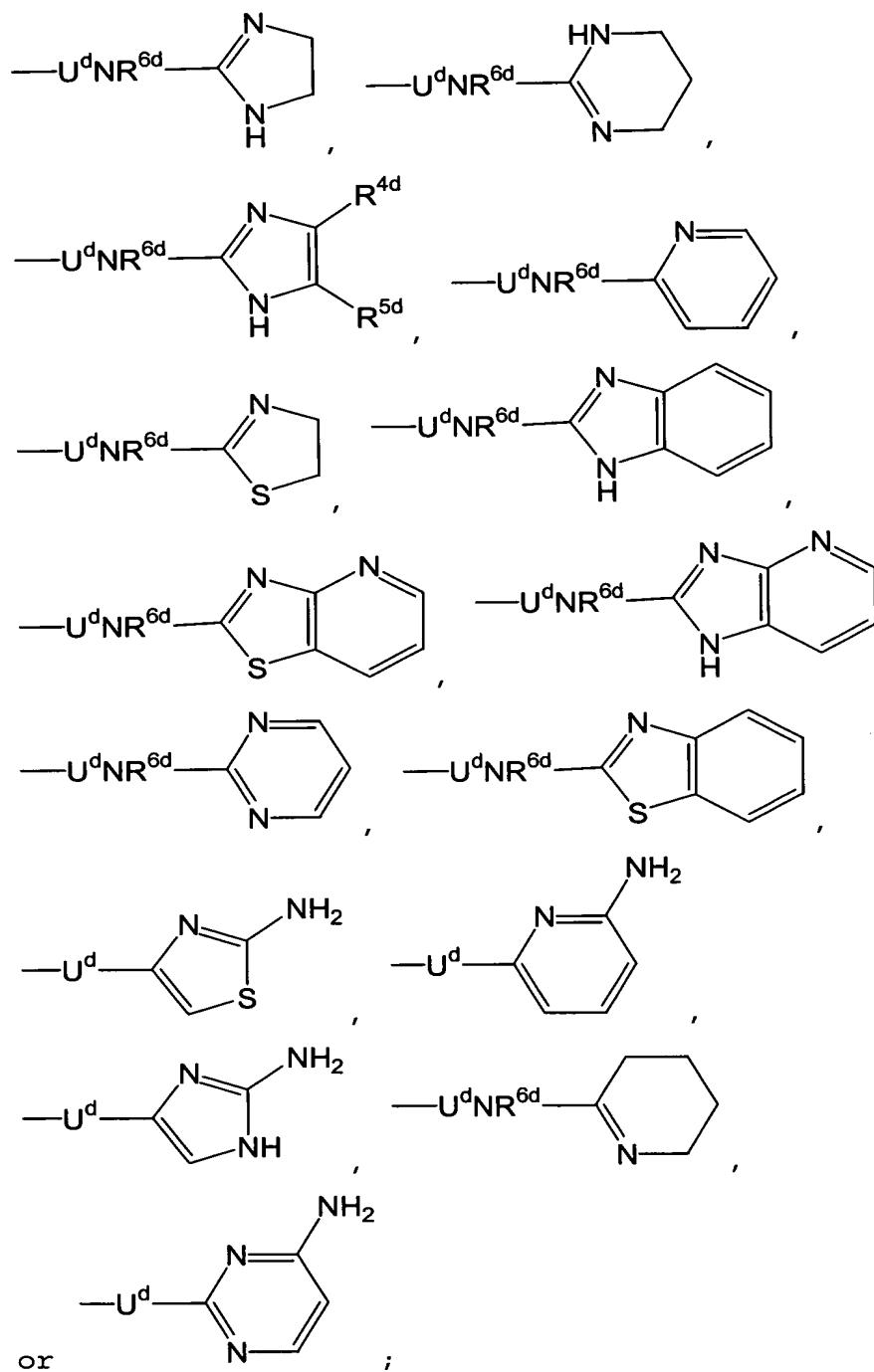
R²⁵ is independently selected at each occurrence from the group: H and C₁-C₃ alkyl.

4. (Original) A compound according to Claim 3, wherein:

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 R^{1de} is selected from:

wherein the above heterocycles are optionally substituted with 0-2 substituents selected from the group: NH₂, halogen, NO₂, CN, CF₃, C₁-C₄ alkoxy, C₁-C₆ alkyl, and C₃-C₇ cycloalkyl;

U^d is -(CH₂)_n-, -(CH₂)_t^dQ^d-(CH₂)_m- or -C(=O)(CH₂)_n-1-, wherein one of the methylene groups is optionally substituted with R^{7d};

R^{7d} is selected from: C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₄-C₁₁ cycloalkylalkyl, aryl, aryl(C₁-C₆ alkyl), heteroaryl, and heteroaryl(C₁-C₆ alkyl);

R^{10d} is selected from: H, R^{1de}, C₁-C₄ alkoxy substituted with 0-1 R^{21d}, halogen, CO₂R^{17d}, CONR^{17d}R^{20d}, C₁-C₆ alkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C₃-C₇ cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C₄-C₁₁ cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, and aryl(C₁-C₆ alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d};

R^{10de} is selected from: H, C₁-C₄ alkoxy substituted with 0-1 R^{21d}, halogen, CO₂R^{17d}, CONR^{17d}R^{20d}, C₁-C₆ alkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C₃-C₇ cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C₄-C₁₁ cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, and aryl(C₁-C₆ alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d};

W^d is -C(=O)-N(R^{13d})-;

x^d is $-\text{CH}(\text{R}^{14d})-\text{CH}(\text{R}^{15d})-$;

R^{13d} is H or CH_3 ;

R^{14d} is selected from:

H, $\text{C}_1\text{-C}_{10}$ alkyl, aryl, or heteroaryl, wherein said aryl or heteroaryl groups are optionally substituted with 0-3 substituents selected from the group consisting of: $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_1\text{-C}_4$ alkoxy, aryl, halo, cyano, amino, CF_3 , and NO_2 ;

R^{15d} is H or R^{16d} ;

y^d is $-\text{COR}^{19d}$;

R^{19d} is selected from:

hydroxy, $\text{C}_1\text{-C}_{10}$ alkoxy,
methylcarbonyloxymethoxy-,
ethylcarbonyloxymethoxy-,
t-butylcarbonyloxymethoxy-,
cyclohexylcarbonyloxymethoxy-,
1-(methylcarbonyloxy)ethoxy-,
1-(ethylcarbonyloxy)ethoxy-,
1-(*t*-butylcarbonyloxy)ethoxy-,
1-(cyclohexylcarbonyloxy)ethoxy-,
i-propyloxycarbonyloxymethoxy-,
t-butyloxycarbonyloxymethoxy-,
1-(*i*-propyloxycarbonyloxy)ethoxy-,
1-(cyclohexyloxycarbonyloxy)ethoxy-,
1-(*t*-butyloxycarbonyloxy)ethoxy-,
dimethylaminoethoxy-,
diethylaminoethoxy-,

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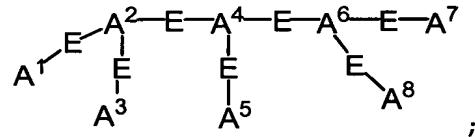
Preliminary Amendment - First Action Not Yet Received

(5-methyl-1,3-dioxacyclopenten-2-on-4-yl)methoxy-,
 (5-(*t*-butyl)-1,3-dioxacyclopenten-2-on-4-yl)methoxy-,
 (1,3-dioxa-5-phenyl-cyclopenten-2-on-4-yl)methoxy-, and
 1-(2-(2-methoxypropyl)carbonyloxy)ethoxy-;

R^{20d} is H or CH_3 ;

m^d is 0 or 1;
 n^d is 1-4;
 t^d is 0 or 1;

C_h is



A^1 is selected from the group: OH, and a bond to L_n ;

A^2 , A^4 , and A^6 are each N;

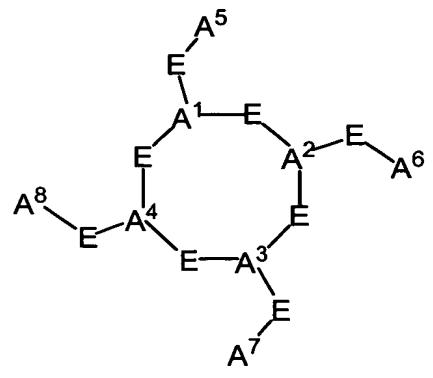
A^3 , A^5 , and A^8 are each OH;

A^7 is a bond to L_n or NH-bond to L_n ;

E is a C_2 alkyl substituted with 0-1 R^{17} ;

R^{17} is =O;

alternatively, C_h is



A^1 is selected from the group: OH and a bond to L_n ;

A^2 , A^3 and A^4 are each N;

A^5 , A^6 and A^8 are each OH;

A^7 is a bond to L_n ;

E is a C_2 alkyl substituted with 0-1 R^{17} ;

R^{17} is =O;

alternatively, C_h is A^1 $E-A^2$;

A^1 is NH_2 or $N=C(R^{20})(R^{21})$;

E is a bond;

A^2 is NHR^{13} ;

R^{13} is a heterocycle substituted with R^{17} , the heterocycle being selected from pyridine and pyrimidine;

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R^{17} is selected from a bond to L_n , $C(=O)NHR^{18}$ and $C(=O)R^{18}$;

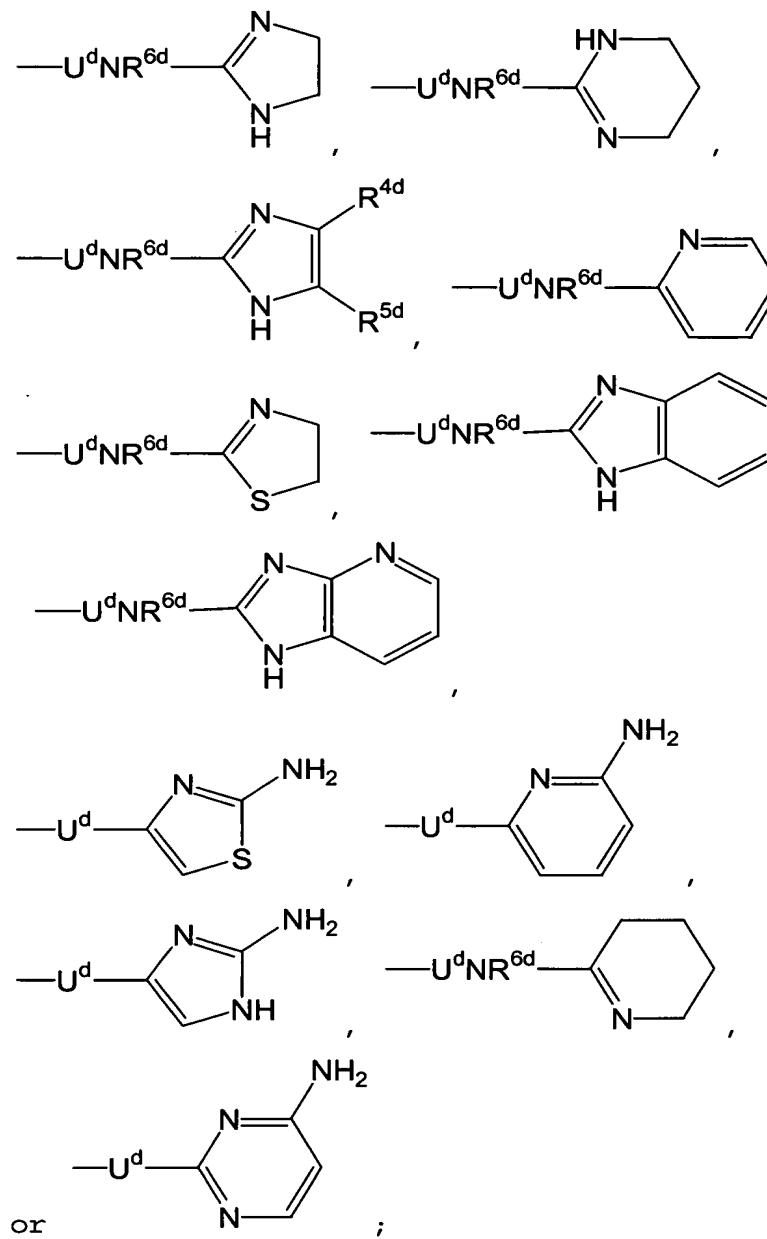
R^{18} is a bond to L_n ;

R^{24} is selected from the group: $-CO_2R^{25}$, $-OR^{25}$, $-SO_3H$, and
 $-N(R^{25})_2$; and,

R^{25} is independently selected at each occurrence from the group: hydrogen and methyl.

5. (Original) A compound according to Claim 4, wherein:

R^{1de} is selected from:



wherein the above heterocycles are optionally substituted with 0-2 substituents selected from the group: NH_2 , halogen,

NO₂, CN, CF₃, C₁-C₄ alkoxy, C₁-C₆ alkyl, and C₃-C₇ cycloalkyl.

6. (Original) A compound according to Claim 2, wherein the compound is selected from the group:

2-(((4-(4-(((3-(2-(3-((6-((1-aza-2-(2-sulfophenyl)vinyl)amino)(3-pyridyl)carbonylamino)propoxy)-ethoxy)ethoxy)propyl)amino)sulfonyl)-phenyl)phenyl)sulfonyl)amino)-3-((1-(3-(imidazole-2-ylamino)propyl)(1H-indazol-5-yl)carbonylamino)propanoic acid;

2-(2-aza-2-((5-(N-(1,3-bis(3-(2-(3-((4-(4-(((1-carboxy-2-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))-carbonylamino)ethyl)amino)sulfonyl)-phenyl)phenyl)sulfonyl)amino)propoxy)-ethoxy)ethoxy)propyl)carbamoyl)propyl)carbamoyl)(2-pyridyl)amino)vinyl)benzenesulfonic acid;

2-((6-((1-aza-2-(sulfophenyl)vinyl)amino)(3-pyridyl)carbonylamino)-4-(N-(3-(2-(2-(3-((4-(4-(((1-carboxy-2-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl)carbonylamino)ethyl)amino)sulfonyl)-phenyl)phenyl)sulfonyl)amino)propoxy)-ethoxy)ethoxy)propyl)carbamoyl)butanoic acid;

3-((1-(3-(imidazole-2-ylamino)propyl)(1H-indazol-5-yl)carbonylamino)-2-((4-(4-(((3-(2-(2-(3-(2-(1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclododecyl)-acetylamino)propoxy)ethoxy)ethoxy)propyl)amino)sulfonyl)-phenyl)phenyl)sulfonyl)amino)propanoic acid;

2-(6-((6-((1-aza-2-(2-sulfophenyl)vinyl)-amino)(3-pyridyl)carbonylamino)hexanoylamino)-3-((1-(3-(imidazol-

2-ylamino)propyl) (1H-indazol-5-yl) carbonylamino) -
propanoic acid;

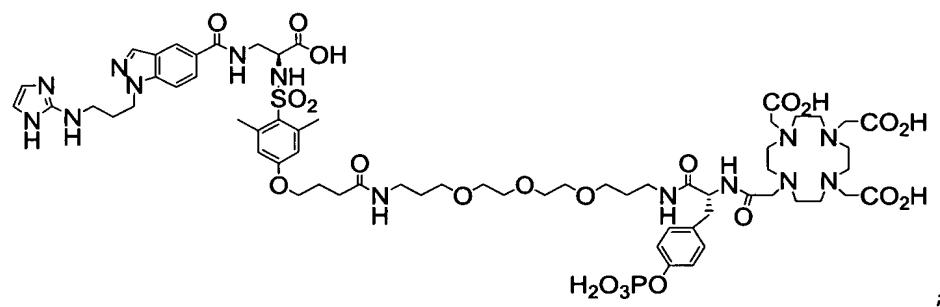
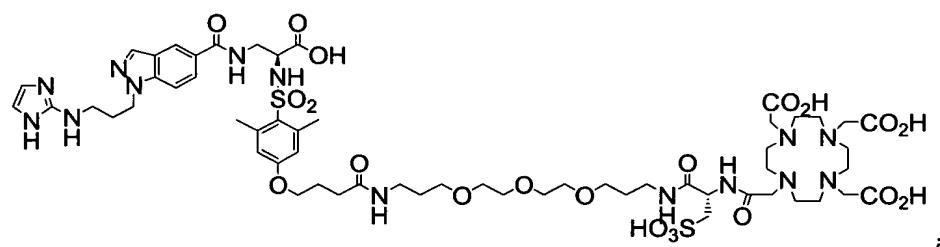
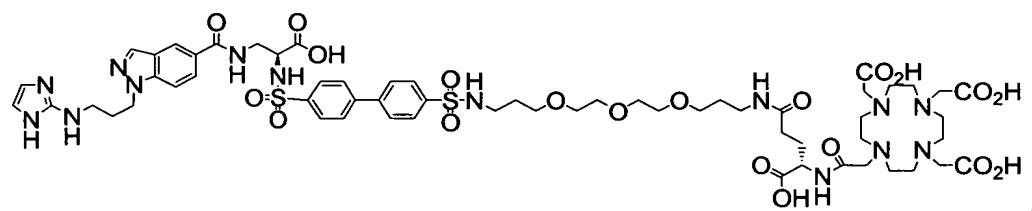
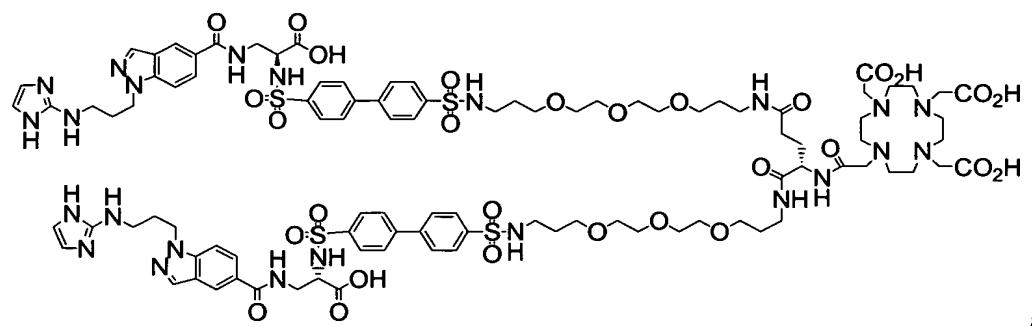
2-((6-((1-aza-2-(2-sulfophenyl)vinyl)-amino) (3-
pyridyl) carbonylamino)-3-((1-(3-(imidazol-2-
ylamino)propyl) (1H-indazol-5-yl) carbonylamino)propanoic
acid;

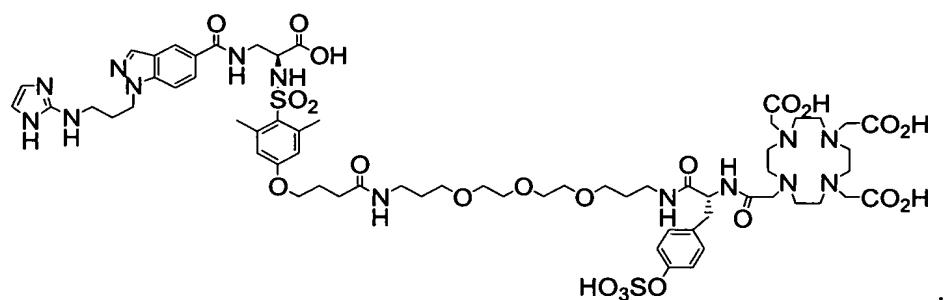
[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl] -
benzenesulfonic acid]-Glu(2-(6-aminohexanoylamino)-3-((1-
(3-(imidazol-2-ylamino)propyl) (1H-indazol-5-yl) carbonyl-
amino)propanoic acid) (2-(6-aminohexanoylamino)-3-((1-
(3-(imidazol-2-ylamino)propyl) (1H-indazol-5-yl) carbonyl-
amino)propanoic acid);

[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl] -
benzenesulfonic acid]-Glu-bis-[Glu(2-(6-
Aminohexanoylamino)-3-((1-(3-(imidazol-2-
ylamino)propyl) (1H-indazol-5-yl) carbonyl-amino)propanoic
acid) (2-(6-aminohexanoylamino)-3-((1-(3-(imidazol-2-
ylamino)propyl) (1H-indazol-5-yl) carbonyl-amino)propanoic
acid)];

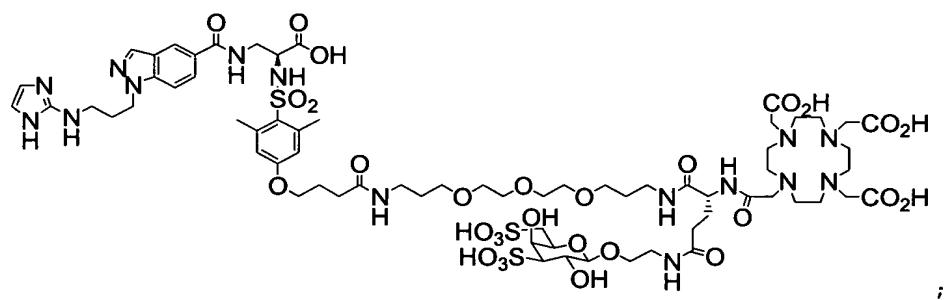
2-(1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)-1-
cyclododecyl)acetyl-{2-(6-aminohexanoylamino)-3-((1-(3-
(imidazol-2-ylamino)propyl) (1H-indazol-5-yl) carbonyl-
amino)propanoic acid};

2-(1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)-1-
cyclododecyl)acetyl-Glu{2-(6-Aminohexanoylamino)-3-((1-
(3-(imidazol-2-ylamino)propyl) (1H-indazol-5-yl) carbonyl-
amino)propanoic acid}{2-(6-Aminohexanoylamino)-3-((1-(3-
(imidazol-2-ylamino)propyl) (1H-indazol-5-yl) carbonyl-
amino)propanoic acid};

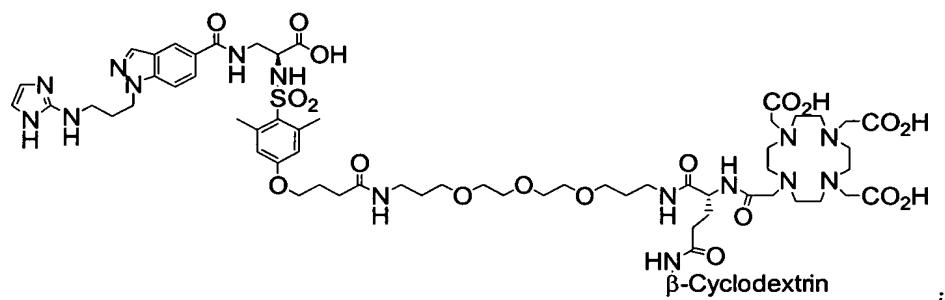




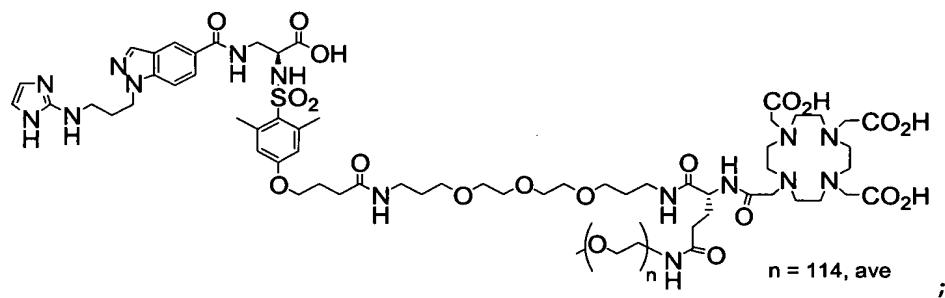
;



;

 β -Cyclodextrin

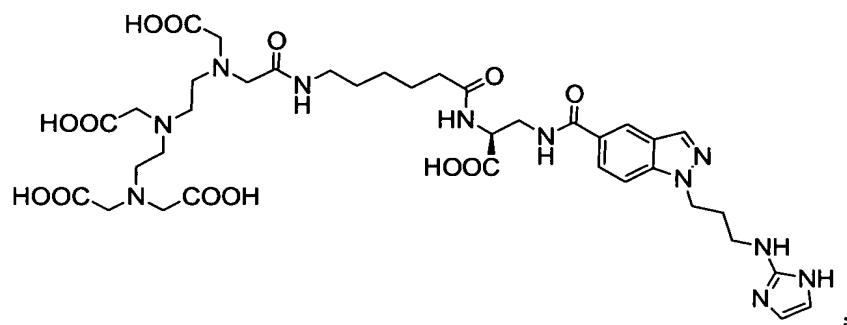
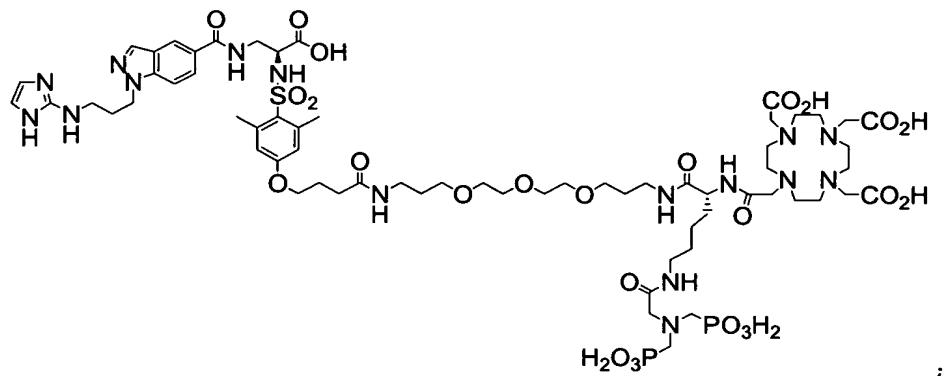
;

 $n = 114, \text{ ave}$

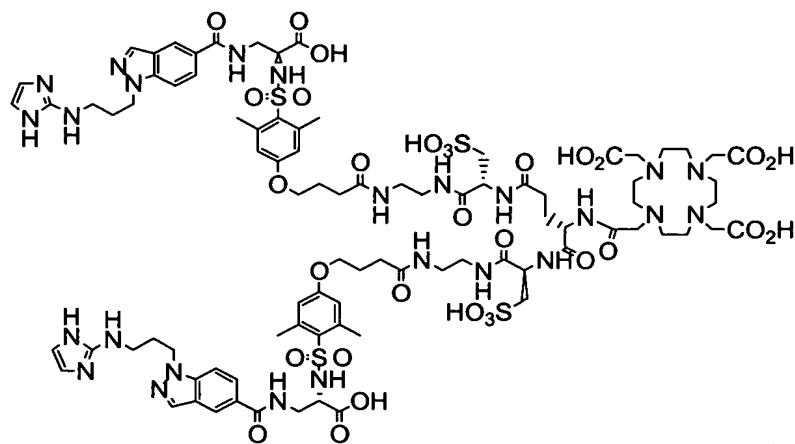
;

2-(((4-(3-(2-(3-(2-(1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclododecylacetyl)amino)-6-aminohexanoyl)amino)propoxy)ethoxy)ethoxy)propyl)-

carbamoyl)propoxy)-2,6-dimethylphenyl)sulfonyl)amino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))-carbonylamino)propionic acid salt;



2-({[4-(3-{N-[2-((2R)-3-Sulfo-2-{2-[1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclododecyl]acetylamino}-propyl)ethyl]carbamoyl}propoxy)-2,6-dimethylphenyl]sulfonyl}amino)(2S)-3-({1-[3-(imidazol-2-ylamino)propyl](1H-indazol-5-yl})carbonylamino)propanoic Acid;



;

2- [({ 4- [4- ({ [2- ((2R) - 3-Sulfo-2- { 2- [1,4,7,10-tetraaza-4,7,10-tris (carboxymethyl) cyclododecyl] - acetyl amino } propyl) ethyl] amino } sulfonyl) phenyl] phenyl] - sulfonyl) amino] (2S) - 3- ({ 1- [3- (imidazol-2-yl amino) propyl] (1H-indazol-5-yl) carbonyl amino } propanoic Acid ;

(4S) - 4- (N- { 1- [N- (2- { 4- ({ [(1S) - 1-carboxy-2- ({ 1- [3- (2-pyridyl amino) propyl] (1H-indazol-5-yl) carbonyl amino } ethyl] amino } sulfonyl) - 3,5-dimethylphenoxy] butanoyl amino } ethyl) carbamoyl] - 3-carboxypropyl } carbamoyl) - 4- { 2- [1,4,7,10-tetraaza-4,7,10-tris (carboxymethyl) cyclododecyl] acetyl amino } butanoic acid ;

(4S) - 4- (N- { 1- [N- (2- { 4- ({ [(1S) - 1-carboxy-2- ({ 1- [3- (imidazol-2-yl amino) propyl] (1H-indazol-5-yl) carbonyl amino } ethyl] amino } sulfonyl) - 3,5-dimethylphenoxy] butanoyl amino } ethyl) carbamoyl] - 3-carboxypropyl } carbamoyl) - 4- { 2- [1,4,7,10-tetraaza-4,7,10-tris (carboxymethyl) cyclododecyl] acetyl amino } butanoic acid ;

(4S)-4-{N-[(1S)-1-(N-{1,3-bis[N-(2-{4-({[(1S)-1-carboxy-2-({1-[3-(imidazol-2-ylamino)propyl](1H-indazol-5-yl)}carbonylamino)ethyl]amino}sulfonyl)-3,5-dimethylphenoxy]butanoylamino}ethyl)carbamoyl]propyl]carbamoyl)-3-carboxypropyl}carbamoyl}-4-{2-[1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclododecyl]acetylamino}hexanoylamino)butanoic acid;

(4S)-4-(N-{1-[N-(2-{4-({[(1S)-1-carboxy-2-({1-[3-(3,4,5,6-tetrahydropyrimidin-2-ylamino)propyl](1H-indazol-5-yl)}carbonylamino)ethyl]amino}sulfonyl)-3,5-dimethylphenoxy]butanoylamino}ethyl)carbamoyl]-3-carboxypropyl}carbamoyl)-4-{2-[1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclododecyl]acetylamino}butanoic acid;

(4S)-4-(N-{1-[N-(2-{4-({[(1S)-1-carboxy-2-({1-methyl-3-[3-(2-3,4,5,6-tetrahydropyridylamino)propyl](1H-indazol-6-yl)}carbonylamino)ethyl]amino}sulfonyl)-3,5-dimethylphenoxy]butanoylamino}ethyl)carbamoyl]-3-carboxypropyl}carbamoyl)-4-{2-[1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclododecyl]acetylamino}butanoic acid;

(4S)-4-(N-{(1S)-1-[N-(2-{4-({[(1S)-1-carboxy-2-({1-[2-(2-3,4,5,6-tetrahydropyridylamino)ethyl](1H-indazol-5-yl)}carbonylamino)ethyl]amino}sulfonyl)-3,5-dimethylphenoxy]butanoylamino}ethyl)carbamoyl]-3-carboxypropyl}carbamoyl)-4-{2-[1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclododecyl]acetylamino}butanoic acid;

(2S)-2-{[(2,6-dimethyl-4-{3-[N-(2-{2-[1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclododecyl]acetyl-amino}ethyl)carbamoyl]propoxy}phenyl)sulfonyl]amino}-3-({2-[2-(2-3,4,5,6-tetrahydropyridylamino)ethyl](2-hydro-1H-indazol-5-yl)}carbonylamino)propanoic acid;

(4S)-4-{N-[(1S)-1-(N-{2-[(4-{[(1S)-1-carboxy-2-({1-[2-(2-3,4,5,6-tetrahydropyridylamino)ethyl] (1H-indazol-5-yl)}carbonylamino)ethyl]amino}sulfonyl)phenyl]phenyl}sulfonyl]amino]ethyl}carbamoyl)-3-carboxypropyl carbamoyl}-4-{2-[1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclododecyl]acetylamino}butanoic acid;

(4S)-4-{N-[(1S)-1-(N-{2-[(4-{[(1S)-1-carboxy-2-({1-[3-(3,4,5,6-tetrahydropyrimidin-2-ylamino)propyl] (1H-indazol-5-yl)}carbonylamino)ethyl]amino}sulfonyl)phenyl}sulfonyl]amino]ethyl}carbamoyl)-3-carboxypropyl carbamoyl}-4-{2-[1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclododecyl]acetylamino}butanoic acid;

(2S)-3-({3-[(imidazol-2-ylamino)methyl]-1-methyl(1H-indazol-6-yl)}carbonylamino)-2-({[4-{[(2-[1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclododecyl]acetylamino)ethyl]amino}sulfonyl]phenyl}sulfonyl)amino)propanoic acid;

3-[(7-{3-[(1E)-1-aza-2-(2-sulfophenyl)vinyl]amino}(3-pyridyl))carbonylamino]propoxy}-1-[3-(imidazol-2-ylamino)propyl] (1H-indazol-5-yl))-carbonylamino] (2S)-2-{{[(2,4,6-trimethylphenyl)sulfonyl]-amino}propanoic acid; and

3-{{[1-[3-(imidazol-2-ylamino)propyl]-7-(3-{2-[1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclododecyl]-acetylamino}propoxy)(1H-indazol-5-yl)]carbonylamino}-2-{{[(2,4,6-trimethylphenyl)sulfonyl]amino}propanoic acid;

or a pharmaceutically acceptable salt form thereof.

7.-57. (cancelled).